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Inventor(s): Andreas N. Dorsel

Serial No.: 10/036,999

Examiner: Betty J. Forman

Filing Date: December 21, 2001

Group Art Unit: 1634

Title: INTERROGATING MULTI-FEATURED ARRAYS

COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria VA 22313-1450

TRANSMITTAL OF REPLY BRIEF

Sir:

Transmitted herewith is the Reply Brief with respect to the Examiner's Answer mailed on 07-10-2006 This Reply Brief is being filed pursuant to 37 CFR 1.193(b) within two months of the date of the Examiner's Answer.

(Note: Extensions of time are not allowed under 37 CFR 1.136(a))

(Note: Failure to file a Reply Brief will result in dismissal of the Appeal as to the claims made subject to an expressly stated new grounds of rejection.)

No fee is required for filing of this Reply Brief.

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Respectfully submitted,

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By

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	First Named Inventor	Dorsel, Andreas N.
	Application Number	10/036,999
	Filing Date	Dec. 21,2001
	Group Art Unit	1634
	Examiner Name	Forman, Betty J.
	Title: *Interrogating Multi-Featured Arrays*	

Sir:

This Reply Brief is in response to the Examiner's Answer mailed by the Office on July 10, 2006.

Please charge any required fees to Deposit Account No. 50-1078, order number 10992125-2.

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REPLY BRIEF

In this Reply Brief, the Appellants address comments made in the Examiner's Answer. The Examiner has raised no new grounds for rejection. The Appellants note that all arguments presented in the prior Appeal Brief still apply with equal force, but are not reiterated in full herein solely in the interest of brevity and for the convenience of the Board.

The comments of the Appellants with regard to certain of the Examiner's findings and assertions in the Examiner's Answer are provided below.

(6) Withdrawn Rejection

The Examiner has withdrawn the rejection of Claims 1, 5, 7, 10 and 11 under 35 U.S.C. § 103(a) over Lehman in view of Brower as in view of Appellant's arguments on pages 7-8 of the Appeal Brief.

(10) Response to Argument

II. Claims 1-5 and 18-20 are not obvious under 35 U.S.C. §103(a) over Bengtsson (U.S. Patent No. 6,078,390) in view of Rava et al. (U.S. Patent No. 5,874,219).

Claim 1

Independent Claim 1 specifies a method of scanning an array of multiple distinct biopolymeric features which includes the step of decreasing power of the interrogating light for a first site on the array package during scanning, wherein the first site is outside an area occupied by the array. In other words, the interrogating light power is decreased at a first site that is not part of the biopolymeric array portion of the array package.

Claim 1 has been rejected over the teachings of Bengtsson and Rava et al. The Examiner asserts that Bengtson teaches each and every element of Claim 1

except that the features of the array are distinct biopolymeric moieties. To remedy this deficiency, the Examiner cites Rava et al.

In maintaining the rejection of Claim 1 over the arguments of the Appellants, the Examiner continues to assert that Bengtsson teaches decreasing power of an interrogating light for a first site on an array package during scanning wherein the first site is outside an area occupied by the array. The Appellants continue to respectfully disagree.

The core of the disagreement between the Appellants and the Examiner is whether the calibration area of Bengtsson constitutes an area that is within an area occupied by the array or whether the calibration area constitutes an area that is outside an area occupied by the array. As argued in the Appeal Brief and discussed below, the Appellants submit that the calibration area of Bengtsson clearly constitutes an area that is within an area occupied by the array.

The first step in the methods disclosed by Bengtsson is locating the position of the array to be scanned, which is described as follows (col. 6, lines 1-13):

> Referring now to FIGS. 1-4, the system 10 automatically sets its sensitivity for a new sample 18 by first, as necessary, locating the micro-array 42 on the sample. To locate the micro-array, the system performs a low-resolution scanning operation with one of the lasers 12 or 14 over the entire sample. This first low-resolution scan operation also provides information from which the user can choose a calibration area (step 402). The system performs this first low resolution scanning operation using a first set of default settings for attenuation and detector gain. In the example, the attenuation level is set to one-half and the detector gain is set to maximum. However, essentially any settings will work.

As can be seen from this section, the power of the interrogating light is not decreased (or increased) during the scan. This step merely allows the array to be located for further scanning operations.

Once locating the array, the user selects a portion of the located array to use as the calibration area, as described in col. 6, lines 23-38, which read:

> Once the position of the micro-array 42 is determined, the user selects a calibration area, which may be the entire micro-array or some portion of the array (step 404). The user preferably selects a portion of the micro-array for which the system produces either saturated signals or signals that indicate the brightest dots. The area may be selected by drawing a box around the area on the screen.

> For some applications the user may be interested solely in the lower levels of fluorescence. Accordingly, the user may select the calibration area from a section of the micro-array that includes the dimmest dots. Calibrating over this dim region means that the signals produced for the brighter regions of the array may be saturated. However, for these applications the signals produced by the brighter dots are of essentially no interest.

As is clear from this section, Bengtsson teaches a calibration area selected from a region that is part of the located array, i.e., <u>within an area occupied by the array</u>. No other calibration area location is disclosed.

In col. 6, lines 38-43, Bengtsson provides an additional way to select a calibration area, stating:

> The array-locating scan operation may be omitted if the user knows the section of the sample to be scanned for calibration. The location would be known if, for example, the user had prepared a set of similar samples and determined the calibration area on a first sample in the set.

In this alternative method, a calibration area can be selected if a user knows the location of the array (e.g., if the user is scanning a number of arrays sequentially which have the same layout). As with the previous section, this section explicitly states that <u>the calibration area is within the area occupied by the array (or "sample")</u>.

In summary, the Appellants submit that the calibration area of Bengtsson clearly is an area that is <u>within</u> an area occupied by the array. As such, it is immaterial whether Bengtsson discloses altering the interrogating light power during a scan of the calibration area because the claimed method is drawn to decreasing power of an interrogating light for a first site on an array package during scanning <u>wherein the first site is outside an area occupied by the array</u>.

As noted in the Appeal Brief, Rava et al. fails to remedy this fundamental deficiency in Bengtsson in teaching the claimed method.

<u>Claims 2-5 and 18-20</u>

Independent Claim 5 specifies an array scanning method in which the interrogating light power is altered for a first site on the array package <u>during scanning</u>, in which the first site is an array feature. Specifically, the interrogating

light power is altered based on the signal emitted from a first site when the interrogating light initially illuminates the first site. Independent Claim 18, and Claims 2-4 and 19-20 that depend therefrom, specify altering power of the interrogating light for a first site based on <u>location of the first site</u> or <u>on a determination that the emitted signal from the first site will be outside a predetermined intensity range absent the altering</u>, wherein the interrogating light power is altered during a row scan of the interrogating light.

In rejecting these claims, the Examiner continues to assert that Bengtsson teaches all the elements of the claimed scanning methods except for scanning arrays of distinct biopolymers. To remedy this deficiency, the Examiner cites Rava et al.

In maintaining the rejection of Claim 1 over the arguments of the Appellants, the Examiner continues to assert that Bengtsson discloses altering the interrogating light power during an array scan as is claimed in Claims 5 and 18 (the only independent claims of this group). The Appellants continue to respectfully disagree.

With regard to Claim 5, the core of the disagreement between the Appellants and the Examiner is whether Bengtsson discloses altering interrogating light power based on a signal emitted from an array feature during the scanning (i.e., when the interrogating light <u>initially illuminates the feature</u>). Claim 5 is thus drawn to real-time alteration of interrogating light power based on emitted signals from an array feature being illuminated. As argued in the Appeal Brief and discussed below, the Appellants submit that Bengtsson fails to disclose such a method.

In essence, Bengtsson discloses two interrogating light power alteration methods. The first is exemplified in col. 6, lines 44-64, which states:

> The system 10 next sets the gain of the detector 20 and the level of attenuation of the attenuator 16 to a second set of default values (step 406). In the example, the system sets the attenuation level to one-half and the gain of the detector to maximum, which are the same as the first set of default values. The system then uses the laser 12 to **re-scan a selected first scan line 301 in the calibration area and produce associated data signals** (step 408). If the data signals associated with N adjacent pixels in the scan line 301 are saturated, the system increases the level of attenuation to reduce the excitation signal power by

> a predetermined factor, in the example, by a factor of two (steps 410, 414). In the example, N is selected between 2 and 8. **The system then re-scans the scan line 301, to determine if the signals associated with N adjacent pixels are still saturated** (step 410). If so, the system determines if the excitation signal power is at a predetermined minimum, in the example one-quarter of the maximum power. If the power is not at the minimum, the system reduces the signal power by a factor of two by again increasing the attenuation level (steps 412, 414). (*emphasis added*)

As can be seen from this section, the power of the interrogating light is altered <u>after completion of scanning a scan line</u> and not in real time as is claimed (i.e., based on the signal emitted form a feature during scanning when the interrogating light initially illuminates the feature). The summary of the invention section also makes clear that this type of interrogating light power alteration is done after completion of scanning a scan line (col. 2, lines 8-22).

The second interrogating light power alteration disclosed in Bengtsson is described in the following passage (col. 8, lines 11-23):

> Referring now to FIG. 5, a system 11 optionally includes a power modulator 500 that controls laser excitation sources 12a and 14a, to essentially turn the lasers 12 and 14 off for some fraction of the time that the system is scanning across a scan line. The system thus performs low-resolution scanning on a per-scan-line basis, that is, pixel-by-pixel, as well as over the calibration area. Specifically, the system turns off the lasers for a fraction of the scanning of each element, or dot, in the scan line. As discussed, **the system need not have determined the locations of the individual elements in the micro-array, as long as the width, or diameters, of the elements are known.** The system then turns the lasers 12 and 14 off for times that translate to a fraction of the width of each of the elements. (emphasis added)

As noted in the Appeal Brief, this section fails to disclose that interrogating light power is altered during a row scan <u>in response to signals emitted from an illuminated feature</u>. The system is merely programmed to alter the power iteratively at intervals that translate to fractions of a width of the elements (so that a portion of each element is illuminated at least once during a scan). The stated purpose of this optional power modulation feature is to further reduce the area scanned during calibration of the system to reduce its impact on the final scan. Thus, in contrast to the assertion of the Examiner, <u>the power modulation in this section is not related in any way to the signal emitted from the feature when illuminated</u>.

Furthermore, it is explicitly stated that the locations of the individual elements need not be known for the power to be altered (in bold, above). The Examiner states in the Examiner's Answer that the above section teaches that "*if the width and diameters [of the elements] are not known, the system **requires** spot detection for calibration*" (emphasis added). The Apellants submit that this section teaches no such thing. Nowhere in Bengtsson, either in this section or any other, is it taught that **any** implementation of this **optional** element **requires** that location of spots be known. It is the Apellant's position that the Examiner has inappropriately inferred this "teaching" from Bengtsson. Why not simply exclude this optional element if the dimensions of the elements are unknown? Bengtsson takes no position regarding this issue and thus provides no teaching either way. Rather, Bengtsson is simply stating that if one need only know the dimensions of the elements to employ this **optional** element: no more, and no less.

The core of the disagreement with regard to Claim 18 is similar to Claim 5. In Claim 18, the power of the interrogating light is altered during a row scan of the interrogating light for a first site based on either: 1) location of the first site; or 2) on a determination that the emitted signal from the first site will be outside a predetermined intensity range absent the altering.

As argued in the Appeal Brief and discussed above, the Appellants submit that Bengtsson fails to disclose altering interrogating light power during a row scan based on the location of the first site or the emitted signal. Specifically, Bengtsson discloses altering interrogating light power in two ways: 1) after completion of a row scan (e.g., as described in col. 6, lines 44-64); and 2) in an iterative fashion during a row scan that is independent of both an emitted signal and location (as described in col. 8, lines 11-23). As such, Bengtsson fails to teach elements of the method claimed in Claim 18 (as recited above).

As noted in the Appeal Brief, Rava et al. fails to remedy these fundamental deficiencies in Bengtsson in teaching the method claimed in Claims 2-5 and 18-20.

In summary, the Appellants submit the combined teachings of Bengtsson et al. and Rava et al. fail establish a *prima facie* case of obviousness because they fail

to teach or suggest each and every element of Claims 1-5 and 18-20. As such, the Appellants respectfully request reversal of this rejection.

III. Claims 7-11 are not obvious under 35 U.S.C. §103(a) over Bengtsson (U.S. Patent No. 6,078,390) in view of Rava et al. (U.S. Patent No. 5,874,219) and Lehman et al. (U.S. Patent No. 5,237,172).

Independent Claim 7 and dependent Claims 8-11 specify a method for array scanning that is similar to that claimed in independent Claims 5 and 18 in that it includes the element of altering the interrogating light power during a row scan of the interrogating light based on location of the first site or on a determination that the emitted signal from the first site will be outside a predetermined range absent the altering. Claim 7 includes the additional element of a "pre-calibration" step in which the interrogating light power is calibrated versus a control signal characteristic from a light system (step (a) of Claim 7).

In rejecting these claims, the Examiner asserts that Bengtsson teaches the elements of the claimed invention except for 1) the pre-calibration step, and 2) scanning addressable arrays of different moieties. To remedy these deficiencies, the Examiner cites Lehman et al., which assertedly teaches pre-calibration as is claimed, and Rava et al., which assertedly teaches scanning addressable arrays of different moieties.

In maintaining this rejection over the arguments of the Appellants, the Examiner continues to assert that Bengtsson, Lehman et al. and Rava et al. teach each and every element of the claimed invention. The core of the disagreement between the Examiner and Appellants is whether Bengtsson teaches altering power of the interrogating light for a first site during a row scan based on location of the first site or on the signal emitted from the first site.

As discussed in detail above and in the Appeal Brief, the Appellants continue to maintain that Bengtsson fails to teach or suggest altering power of the interrogating light for a first site during a row scan based on location of the first site

or on the signal emitted from the first site and that Lehman et al. and Rava et al. fail remedy these fundamental deficiencies.

As such, the Appellants respectfully request that this rejection be reversed.

SUMMARY

The Appellants respectfully request that the rejections of Claims 1-5, 7-11 and 18-20 under 35 U.S.C. § 103(a) be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,
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